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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/169,048	10/08/1998	WILLIAM D. HUSE	P-IX-3280	5187

23601 7590 10/07/2003

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EXAMINER	
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ART UNIT	PAPER NUMBER
1639	

DATE MAILED: 10/07/2003

31

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No. 09/169,048	Applicant(s) Huse et al
	Examiner Maurie G. Baker, Ph.D.	Art Unit 1639

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *THREE* MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136 (a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1) ☒ Responsive to communication(s) filed on *Jul 14, 2003* .

2a) ☒ This action is **FINAL.** 2b) ☐ This action is non-final.

3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

Disposition of Claims

4) ☒ Claim(s) *10-45* is/are pending in the application.

4a) Of the above, claim(s) *19-38, 42, 44, and 45* is/are withdrawn from consideration.

5) ☐ Claim(s) _____ is/are allowed.

6) ☒ Claim(s) *10-18, 39-41, and 43* is/are rejected.

7) ☐ Claim(s) _____ is/are objected to.

8) ☐ Claims _____ are subject to restriction and/or election requirement.

Application Papers

9) ☐ The specification is objected to by the Examiner.

10) ☐ The drawing(s) filed on _____ is/are a) ☐ accepted or b) ☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13) ☐ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a) ☐ All b) ☐ Some* c) ☐ None of:

1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____ .
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

*See the attached detailed Office action for a list of the certified copies not received.

14) ☒ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

a) ☐ The translation of the foreign language provisional application has been received.

15) ☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s). _____
4) ☐ Interview Summary (PTO-413) Paper No(s). _____
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other:

DETAILED ACTION

1. The Response filed on July 14, 2003 (Paper No. 30) is acknowledged. No claims were cancelled, added or amended in this response. Therefore, claims 10-45 are currently pending.

2. Claims 42, 44 and 45 do not read on the elected species of ligands. Therefore claims 42, 44 and 45 remain withdrawn from further consideration by the examiner, 37 CFR 1.142(b), as being drawn to non-elected species, there being no allowable generic claim. Also, claims 19-38 remain withdrawn from further consideration by the examiner, 37 CFR 1.142(b), as being drawn to non-elected inventions. Election was made **without** traverse in Paper No. 14 (for Groups III-V, claims 19-38). A complete reply to the final rejection must include cancellation of nonelected claims or other appropriate action (37 CFR 1.144). See MPEP § 821.01.

3. Therefore, claims 10-18, 39-41 and 43 are currently under examination.

Maintained Rejections
Claim Rejections - 35 USC § 112

4. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

5. Claims 10-18, 40, 41 and 43 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. This is a new matter rejection.

The specification as originally filed does not provide support for the invention as now claimed. The instant claims contain the limitations "two or more receptors" or "five or more receptors". After close inspection of the instant specification, the examiner deems that these limitations are not supported. The examiner does not believe there is sufficient support for the *specific* recitation of screening a "collective ligand variant population" against a population of "two or more receptors" or "five or more receptors". Applicant points to various portions of the instant specification; however, this is dealing only with the size of the population, not the number of receptors it binds.

The question is what applicants had possession of at the time of filing. There is ***no*** indication in the instant case that applicants had possession of the concept of screening the claimed "collective ligand variant population" for binding against "two or more receptors" or "five or more receptors".

An objective standard for determining compliance with the written description requirement is, "does the description clearly allow persons of ordinary skill in the art to recognize that he or she invented what is claimed." *In re Gosteli*, 872 F.2d 1008, 1012, 10 USPQ2d 1614, 1618 (Fed. Cir. 1989). It is completely unclear that the

description as filed supports the limitations of screening populations of "two or more receptors" or "five or more receptors". Note that a broad generic disclosure is **not** sufficient support for a *specific* entity within the class.

Response to Arguments

6. Applicant's arguments filed July 14, 2003 have been fully considered but are not found persuasive. The examiner's rationale is set forth below.

7. Applicant states that "the specification need not provide literal support for the claim language" (Response, page 2). While this may be true, it must be clear from the description that the concepts as claimed were contemplated. An objective standard for determining compliance with the written description requirement is, "does the description clearly allow persons of ordinary skill in the art to recognize that he or she invented what is claimed." *In re Gosteli*, 872 F.2d 1008, 1012, 10 USPQ2d 1614, 1618 (Fed. Cir. 1989). This applies to new matter situations as well as written description of originally filed claims.

8. Applicant then cites several pieces of case law and points to several places in the instant specification for support. The portions of the instant specification to which applicant points for support (Response, pages 4-5) are not deemed sufficient. These citations only support the size of populations *in general* (instant specification, page 9, line 26 – page 10, line 11) and the concept that "a population of receptors can be screened" (instant specification, page 12, line 26). Nowhere is *the specific disclosure of screening a "collective*

ligand variant population" against a population of "two or more receptors" or "five or more receptors" disclosed. For these reasons, the above claims remain rejected as unsupported by the specification as originally filed.

Maintained Rejections
Claim Rejections - 35 USC § 112

9. Claims 10-18, 39-41 and 43 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

To satisfy the written description requirement, an applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession of the invention. Applicant's claims are directed to a method of determining binding of a "ligand" to one or more "receptors". The claims use generic terminology such as "collective ligand variant population", "binding activity" and "optimal binding affinity". These terms are defined in the instant disclosure but the definitions are very broad.

The specification discloses **no** examples of carrying out such a method (the only example given appears to be for the opposite case scenario). These ligands and receptors could encompass very different moieties such as peptides, oligonucleotides or other organic molecules. Also, claims 15 and 16 require specific techniques of producing the ligands (recombinant expression in melanophore cells) and claim 17 and 39 require tagging. None of these techniques are adequately described in the

instant disclosure. There are **no** examples of producing ligands by recombinant expression in melanophore cells and **no** examples of tagging such ligands whatsoever.

Thus, the disclosure simply does not provide adequate support to show possession of the claimed invention. The disclosure is neither representative of the claimed genus, nor does it represent a substantial portion of the claimed genus. Moreover, the claimed genus encompasses members which are yet to be prepared or envisioned. This further evidences that instant disclosure does not constitute support for the claimed genus or a substantial portion thereof.

Response to Arguments

10. Applicant's arguments filed July 14, 2003 have been fully considered but are not found persuasive. The examiner's rationale is set forth below. Please also see Response to Arguments set forth in paragraphs 20-28 below.

11. Applicant argues that the claims are adequately described and sets forth various citations/definitions from the instant specification concerning the terms discussed in the rejection (see Response, pages 5-7). The examiner acknowledged these definitions in the rejection above but stated that they were *very broad*. The "collective ligand variant population" recited in the claims could encompass a virtually unlimited number of compounds. This is because the instant claims give ***no structure*** for the ligand itself and no structural information as to the specific "variant". Thus the claims could encompass an

infinite number of variations. As also stated above, the examiner pointed out that the specification discloses **no** examples of the claimed "collective ligand variant population".

12. Applicant states that methods are claimed and that the claimed methods "can be practiced with ligands having a variety of structures" (Response, page 6). However, it appears that the "collective ligand variant population" is essential to the claimed method and thus it must be adequately described. See also paragraphs 16-18 below.

13. Applicant argues that no working examples are necessary and that the provided example (which is for the opposite case scenario than what is instantly claimed), provides adequate support (see Response, pages 7-8). While an example is indeed not required, lack of a working example, however, is a factor to be considered, especially in a case involving an unpredictable and undeveloped art (see below). Also, one of ordinary skill would not necessarily expect to be able to extrapolate the disclosed example (to the opposite case scenario) as far as its applicability to the instant claims.

14. Also, the examiner deems the art to be unpredictable. The "predictability or lack thereof" in the art refers to the ability of one skilled in the art to extrapolate the disclosed or known results to the claimed invention. If one skilled in the art can readily anticipate the effect of a change within the subject matter to which the claimed invention pertains, then there is predictability in the art. On the other hand, if one skilled in the art cannot readily anticipate the effect of a change within the subject matter to which that claimed invention

pertains, then there is lack of predictability in the art. Additionally, the Board has held on the issue of unpredictability that "... the unpredictability of an art area alone may be enough to create a reasonable doubt as to the accuracy of statements in the specification." *Ex parte Singh*, 17 U.S.P.Q.2d 1714,1716 (B.P.A.I. 1990).

15. Applicant refers to various teachings from the instant specification and the prior art to support their argument that the claims are adequately described (Response, pages 8-10). First, it is noted that these arguments are not commensurate in scope with the claims. That is, for example, with respect to the arguments regarding ligand DNA constructs (Response, page 9), the independent claims are not limited to such ligands. Also, although the claims are interpreted in light of the specification, limitations from the specification are not read into the claims. See *In re Van Geuns*, 988 F.2d 1181, 26 USPQ2d 1057 (Fed. Cir. 1993). Moreover, when there is little to no disclosure in the instant specification of the starting material or conditions under which claimed process can be carried out, this failure cannot be rectified by asserting that all disclosure related to the process is within skill of art. *Genentech Inc. v. Novo Nordisk A/S* (CA FC) 42 USPQ2d 1001 (3/13/1997)

16. With respect to adequate disclosure of the scope of the presently claimed generic applicant is referred to the discussion in *University of California v. Eli Lilly and Co.* (U.S. Court of Appeals Federal Circuit (CAFC) 43 USPQ2d 1398 7/22/1997 Decided July 22, 1997; No. 96-1175) regarding disclosure. For adequate disclosure, like enablement, requires representative examples which provide reasonable assurance to one skilled in the art that the

compounds falling within the scope both possess the alleged utility and additionally demonstrate that applicant had possession of the full scope of the claimed invention. See *In re Riat* (CCPA 1964) 327 F2d 685, 140 USPQ 471; *In re Barr* (CCPA 1971) 444 F 2d 349, 151 USPQ 724 (for enablement) and *University of California v. Eli Lilly and Co* cited above (for disclosure). The more unpredictable the art the greater the showing required (e.g. by "representative examples") for both enablement and adequate disclosure. Again, no working examples reading on the instant claims have been provided.

17. The language of the specification should describe the claimed invention so that one skilled in the art can recognize what is claimed. A description of a compound in terms of its function fails to distinguish the compound from others having the same activity or function. A description of what a material does, rather than of what it is, usually does not suffice. The disclosure must allow one skilled in the art to visualize or recognize the identity of the subject matter purportedly described. *University of California v. Eli Lilly and Co.* (U.S. Court of Appeals Federal Circuit (CAFC) 43 USPQ2d 1398 7/22/1997 Decided July 22, 1997; No. 96-1175).

18. Lastly, an objective standard for determining compliance with the written description requirement is, "does the description clearly allow persons of ordinary skill in the art to recognize that he or she invented what is claimed." *In re Gosteli*, 872 F.2d 1008, 1012, 10 USPQ2d 1614, 1618 (Fed. Cir. 1989). The examiner maintains because of the breadth of the claims, the unpredictability of the art and the lack of any working examples the above

standard is not met. Thus the above rejection of claims 10-18, 39-41 and 43 under 35 U.S.C. 112, first paragraph is deemed to be proper.

Maintained Rejections
Claim Rejections - 35 USC § 112

19. Claims 10-18, 39-41 and 43 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

There are many factors to be considered when determining whether there is sufficient evidence to support a determination that a disclosure does not satisfy the enablement requirement and whether any necessary experimentation is "undue". These factors include, but are not limited to:

(1) the breadth of the claims;
(2) the nature of the invention;
(3) the state of the prior art;
(4) the level of one of ordinary skill;
(5) the level of predictability in the art;
(6) the amount of direction provided by the inventor;
(7) the existence of working examples; and
(8) the quantity of experimentation needed to make or use the invention based on the content of the disclosure.

See *In re Wands*, 858 F.2d 731, 737, 8 USPQ2d 1400, 1404 (Fed. Cir. 1988).

The breadth of the claims and the nature of the invention: The claims are drawn to a method of determining binding of a "ligand" to one or more "receptors". No limitations on the specific structure of the ligand or receptor are given and, as such, this could read on a wide variety of structures. The invention is such that each of the

components must be present in operable form for successful practice of the invention. For example, the ligand must bind the receptor and the binding must be able to be detected. The state of the prior art and the level of predictability in the art: Ligand/receptor binding pairs were well-known in the art at the time of the invention (see art rejection below); however, only limited numbers of such pairs were known and the specification gives no guidance to permit one of skill in the art to devise strategies for determining binding of *any* such pair of molecules and for the creation of the claimed "collective ligand variant population". The structures of possible variants are sufficiently diverse that one of ordinary skill would not be able to predict their structures, and thus the methodology for determining binding of such. Also, claims 15 and 16 require specific techniques of producing the ligands (recombinant expression in melanophore cells) and claim 17 and 39 require tagging. All of these techniques are unpredictable in the art. One of ordinary skill would not know, a priori, how to make such a ligand by the claimed method and also how to tag such a ligand with an "identifiable tag". Specifically, in regard to claims 15 and 16, it was known in the art at the time of filing how to make *receptors* using melanophore cells (see US 5,462,856, on PTO-1449, Examples 1-6 and claims), but not how to make *ligands* in such a manner. With regard to claims 17 and 39, adding tags to the ligands adds to the unpredictability of the claimed method since this type of synthesis requires high efficiency and is further complicated by carryover, cross-reactions, etc., all of which are acknowledged issues in the art. Each must be dealt with in the optimization of a synthesis scheme. A review article published by Janda discusses

these issues (see Proc. Natl. Acad. Sci. Vol. 91 pp. 10779-10785, November 1994. See especially page 10782-10785). The level of one of ordinary skill: The level of skill would be high, most likely at the Ph.D. level. However, such persons of ordinary skill in this art, *given its unpredictability*, would have to engage in undue (non-routine) experimentation to carry out the invention as claimed. The amount of direction provided by the inventor and the existence of working examples: Applicants have provided **no** working examples of the claimed method, for both the generic embodiments (claims 10-14 and 18) or the specific embodiments (claims 15-17, 39-41 and 43). The state of the prior art is such that one of ordinary skill could not predict how to produce the required ligands (i.e. "collective ligand variant population") and practice the claimed method of determining binding as required by the instant claims. The issue here is the breadth of the claims in light of the predictability of the art as determined by the number of working examples, the skill level of the artisan and the guidance presented in the instant specification and the prior art of record. Also note that "in applications directed to inventions in arts where the results are unpredictable, the disclosure of a single species usually does not provide an adequate basis to support generic claims." *In re Soll*, 97 F.2d 623, 624, 38 USPQ 189, 191 (CCPA 1938). "In cases involving unpredictable factors, such as most chemical reactions and physiological activity, more may be required." *In re Fisher*, 427 F.2d 833, 839, 166 USPQ 18, 24 (CCPA 1970). The quantity of experimentation needed to make or use the invention based on the content of the disclosure: The instant specification does not provide to one skilled in the art a

reasonable amount of guidance with respect to the direction in which the experimentation should proceed in carrying out the practice of the claimed invention due to the deficiencies described above. Note that there must be sufficient disclosure, either through illustrative examples or terminology, to teach those of ordinary skill how to make and use the invention as broadly as it is claimed. *In re Vaeck*, 947 F.2d 488, 496 & n.23, 20 USPQ2d 1438, 1445 & n.23 (Fed. Cir. 1991). Therefore, it is deemed that further research of an unpredictable nature would be necessary to make or use the invention as claimed.

Response to Arguments

20. Applicant's arguments filed July 14, 2003 have been fully considered but are not found persuasive. The examiner's rationale is set forth below. Please also see Response to Arguments set forth in paragraphs 10-18 above.

21. Applicant argues that the claims are enabled and sets forth various citations/definitions from the instant specification concerning the terms discussed in the rejection (see Response, page 10). However, the terms/methods described by applicant are set forth in only the broadest terms. As stated in the rejection, no limitations on the specific structure of the ligand or receptor are given and, as such, this could read on a wide variety of structures. The invention is such that each of the components must be present in operable form for successful practice of the invention. For example, the ligand must bind the receptor and the binding must be able to be detected.

22. As stated above (paragraph 14), the examiner deems the art to be unpredictable. In cases involving unpredictable factors, such as most chemical reactions and physiological activity, the scope of enablement obviously varies inversely with the degree of unpredictability of the factors involved. See *In re Fisher*, 57 CCPA 1099,427 F.2d 833,839,166 USPQ 18,24(1970). Additionally, the Board has held on the issue of unpredictability that "... the unpredictability of an art area alone may be enough to create a reasonable doubt as to the accuracy of statements in the specification." *Ex parte Singh*, 17 U.S.P.Q.2d 1714,1716 (B.P.A.I. 1990).

23. Applicant argues that the instant specification provides sufficient teachings regarding structure and function of the claimed "collective ligand variant population" (see, for example, Response page 11, bottom through page 12, top). However, the examiner's position is that the instant specification does not provide to one skilled in the art a reasonable amount of guidance with respect to the direction in which the experimentation should proceed in making and using the claimed invention. Most importantly, ***the instant specification fails to identify that structure which is required for the claimed activity***. In the absence of such guidance, a practitioner of the art would have to resort to a substantial amount of experimental trial and error to produce a "collective ligand variant population" that has the required functional limitations. This trial and error would clearly constitute undue experimentation.

24. Applicant also argues that one of ordinary skill would know how to tag the claimed ligands (Response, pages 12-14). The examiner respectfully disagrees as such processes were unpredictable and highly dependent on compound structure (as evidenced by the cited Janda reference). The same is true for recombinant expression of the ligand variant population in cells (instant claims 15 and 16). Again, ***no structure*** for the instant "collective ligand variant population" is provided. Note that "if there is no disclosure of any starting material or of any conditions under which claimed process can be carried out, undue experimentation is required, and there is failure to meet enablement requirement that cannot be rectified by asserting that all disclosure related to process is within skill of art." *Genentech Inc. v. Novo Nordisk A/S* (CA FC) 42 USPQ2d 1001 (3/13/1997).

25. The art citations with respect to unpredictability (Response, page 14, top) are not commensurate in scope with the claims. Applicant also argues that the tagging and expression techniques are routine in the art. However, the rule that the specification need not disclose what is well known in art means only that omission of minor details does not cause the specification to fail to meet the enablement requirement, and is not a substitute for a basic enabling disclosure; if there is no disclosure of any starting material or of any conditions under which claimed process can be carried out, undue experimentation is required, and there is failure to meet enablement requirement that cannot be rectified by asserting that all disclosure related to the process is within the skill of the art. *Genentech Inc. v. Novo Nordisk A/S* (CA FC) 42 USPQ2d 1001 (3/13/1997).

26. Applicant again argues that that no working examples are necessary and that the provided example (which is for the opposite case scenario than what is instantly claimed), provides adequate support (see Response, page 14). While an example is indeed not required, lack of a working example, however, is a factor to be considered, especially in a case involving an unpredictable and undeveloped art (see above). Also, one of ordinary skill would not necessarily expect to be able to extrapolate the disclosed example (to the opposite case scenario) as far as its applicability to the instant claims.

27. Please also note that arguments of counsel alone cannot take the place of evidence in the record once an examiner has advanced a reasonable basis for questioning the disclosure. See *In re Budnick*, 537 F.2d at 538, 190 USPQ at 424; *In re Schulze*, 346 F.2d 600, 145 USPQ 716 (CCPA 1965); and *In re Cole*, 326 F.2d 769, 140 USPQ 230 (CCPA 1964). For example, in a case where the record consisted substantially of arguments and opinions of applicant's attorney, the court indicated that factual affidavits could have provided important evidence on the issue of enablement. See *In re Knowlton*, 500 F.2d at 572, 183 USPQ at 37, and *In re Wiseman*,596 F.2d 1019, 201 USPQ 658 (CCPA 1979).

28. For these reasons and the reasons of record, the instant claims lack enablement and the rejection above is deemed proper.

Maintained Rejections
Claim Rejections - 35 USC § 112

29. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

30. Claims 10, 17, 39 and 40 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

A. Claims 10, 17 and 39 recite that the ligand variants are tagged. This limitation is confusing and thus renders the claims indefinite. It is unclear as to applicant's intent since the structure of the ligand variant is not set forth in the claims. Specifically, the claims are incomplete for omitting essential structural cooperative relationships of elements, such omission amounting to a gap between the necessary structural connections. See MPEP § 2172.01. The omitted structural cooperative relationships are: how the claimed tags are associated with the ligands. Note that the elected species of ligand is polypeptide and that claim 39 recites "peptide tags". This provides further confusion as it is unclear how the polypeptide ligands are to be tagged with "peptide tags".

B. Claim 40 recites "organic-derived compound ligands". The term "organic-derived" is a relative term which renders the claim indefinite. The term is not defined by the claim, the specification does not provide a standard for ascertaining the requisite degree, and one of ordinary skill in the art would not be reasonably apprised of the scope of the invention.

Response to Arguments

31. Applicant's arguments filed July 14, 2003 have been fully considered but are not found persuasive. The examiner's rationale is set forth below.

32. Applicant argues that the claims are clear and definite. Regarding A above, applicant argues that the explicit recitation of the structure of the ligand or ligand variant is not required. However, the examiner maintains that the claims are incomplete for omitting essential structural cooperative relationships of elements, such omission amounting to a gap between the necessary structural connections. Whether the tagged ligand variants are claimed *per se* or they are used in a method, their composition should be clear.

33. Regarding B above, applicant argues that the term "organic-derived" would be clear to one of ordinary skill. However, the examiner maintains that this is a relative term and thus renders the claim indefinite for the reasons set forth above. Also note the following from MPEP 2173.02 with respect to both A and B above: If the scope of the invention sought to be patented cannot be determined from the language of the claims with a reasonable degree of certainty, a rejection of the claims under 35 U.S.C. 112, second paragraph is appropriate. *In re Wiggins*, 488 F.2d 538, 179 USPQ 421 (CCPA 1973). For these reasons the rejections under 35 U.S.C. 112, second paragraph are maintained.

Maintained Rejections
Claim Rejections - 35 USC § 102

34. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States

35. Claim 41 is rejected under 35 U.S.C. 102(b) as being anticipated by Combs et al (JACS, January 1996, Vol. 118, No. 1, pp. 287-288).

Combs et al disclose a method for using a "a library of ligands that direct non-peptide binding elements into the specificity pocket of SH3 proteins" (see Figure 1). These ligands comprise two binding sites; "a common low affinity biasing sequence PLPPLP" and 32 "capping reagents" that have the potential to bind in the specificity pocket (see page 287). As the ligands of the reference contain the sequence PLPPLP, they are deemed to read on polypeptide ligands and the claimed "collective ligand variant population". The SH3 domain from the protein kinase Src is the receptor. The compounds were assayed against this receptor and at least 7 ligands were identified that bind (see Figure 3 and Table 1). Ligand 1A was also measured against the SH3 domain in the p85 component of PI3K and did show binding for this domain (a second receptor), although it showed selectivity for Src SH3 (see page 288, 2nd column). The reference discloses that the compounds of the library were tagged and then decoded to find an optimal binding ligand (Figure 3 and Table 1) and the binding

of the library compounds (ligands) to the receptor was performed in three stages (see page 287, 2nd column, bottom and Supplemental pages 1-3).

Response to Arguments

36. Applicant's arguments filed July 14, 2003 have been fully considered but are not found persuasive. The examiner's rationale is set forth below.

37. Applicant argues that since the testing of Combs is carried out in a subsequent manner, the reference does not anticipate the claims (Response, page 16-17). In response to applicant's argument that the references fail to show certain features of applicant's invention, it is noted that the features upon which applicant relies (i.e., simultaneous testing of the entire population) are not recited in the rejected claim(s). Although the claims are interpreted in light of the specification, limitations from the specification are not read into the claims. See *In re Van Geuns*, 988 F.2d 1181, 26 USPQ2d 1057 (Fed. Cir. 1993).

38. For this reason and the reasons of record, the above rejection under 35 U.S.C. 102(b) is maintained.

Maintained Rejections
Claim Rejections - 35 USC § 103

39. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

40. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(f) or (g) prior art under 35 U.S.C. 103(a).

41. Claims 10-14, 17, 18, 40 and 43 are rejected under 35 U.S.C. 103(a) as being unpatentable over Combs et al (JACS, January 1996; of record).

Combs et al teach a method for using a "a library of ligands that direct non-peptide binding elements into the specificity pocket of SH3 proteins" (see Figure 1). These ligands comprise two binding sites; "a common low affinity biasing sequence PLPPLP" and 32 "capping reagents" that have the potential to bind in the specificity pocket (see page 287). As the ligands of the reference contain the sequence PLPPLP, they are deemed to read on polypeptide ligands (i.e. instant claims 40 and 43) and the claimed "collective ligand variant population". The SH3 domain from the protein kinase Src is the receptor. The compounds were assayed against this receptor and at least 7 ligands were identified that bind (see Figure 3 and Table 1). Ligand 1A was

also measured against the SH3 domain in the p85 component of PI3K and did show binding for this domain (a second receptor), although it showed selectivity for Src SH3 (see page 288, 2nd column). The reference teaches that the compounds of the library were tagged and then decoded to find an optimal binding ligand (Figure 3 and Table 1) and the binding of the library compounds (ligands) to the receptor was performed in three stages (see page 287, 2nd column, bottom and Supplemental pages 1-3). This reads directly on the limitations of the instant claims 11-14, 17 and 18.

Combs et al lacks the specific teaching of testing their library of ligands against "five or more receptors".

However, the reference does teach testing the library against *two* receptors and to test the library against further receptors would be obvious to one of ordinary skill. Note that "[w]here the general conditions of a claim are disclosed in the prior art, it is not inventive to discover the optimum or workable ranges by routine experimentation." *In re Aller*, 220 F.2d 454, 456, 105 USPQ 233, 235 (CCPA1955).

Therefore, it would have been *prima facie* obvious to one of ordinary skill in the art at the time of the invention to test the library of Combs et al against any number of receptors. One would be motivated to do so in order to identify ligands that particularly bind a desired receptor. Combs et al teaches that their methodology is effective for identification of ligands for SH3 domains (of which there are several) and further that their methodology "is expected to be applicable to the discovery of ligands to proteins in general" (page 288, 2nd column, bottom).

Response to Arguments

42. Applicant's arguments filed July 14, 2003 have been fully considered but are not found persuasive. The examiner's rationale is set forth below.

43. Applicant makes the same argument on page 17 of the Response with respect to the 103 rejection as was made for the 102 rejection. The examiner maintains that the Combs reference anticipates claim 41 for the reasons set forth in paragraphs 36-38 above. Thus, the examiner also maintains that the Combs reference renders claims 10-14, 17, 18, 40 and 43 obvious for the same reasons and reasons of record.

Status of Claims/ Conclusion

44. No claims are allowed.

45. **THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory

period for reply expire later than SIX MONTHS from the mailing date of this final action.

46. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Maurie Garcia Baker, Ph.D. whose telephone number is (703) 308-0065. The examiner is on an increased flextime schedule but can normally be reached on Monday-Thursday and alternate Fridays from 9:30 to 7:00.

47. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Andrew J. Wang, can be reached at (703) 306-3217. The fax phone number for the organization where this application or proceeding is assigned is (703) 872-9306. Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-0196.

Maurie Garcia Baker, Ph.D.
October 5, 2003

MAURIE GARCIA BAKER PH.D
PRIMARY EXAMINER